Panacea Journal of Pharmacy and Pharmaceutical Sciences 2023:12(4), 12-21
International Journal

Panacea Journal of Pharmacy and Pharmaceutical Sciences
ISSN: 2349 7025

PJPPS
Panacea Research Library
http://internationaljournal.org.in/journal/index.php/pjpps

Original Research Article **Volume 12 Issue 4** **Oct-Dec 2023**

OPTIMIZATION OF METOCLOPRAMIDE FAST-DISSOLVING TABLETS: FORMULATION, DEVELOPMENT, AND EVALUATION

Shivam Upadhyay, Reena Shende, Teena Parmar, Chandani Gupta,

Dr. Satkar Prasad

RKDF School of Pharmaceutical Sciences, Bhopal (M.P.)

Corresponding Author: shivamupadhyay35093@gmail.com

Abstract

Metoclopramide, a widely utilized antiemetic and gastroprokinetic drug, is renowned for its effectiveness in managing nausea, vomiting, and gastrointestinal disorders. However, conventional Metoclopramide tablets face limitations related to slow dissolution and delayed onset of action. To overcome these challenges and enhance patient compliance, this study focuses on the formulation, development, and evaluation of Metoclopramide fast-dissolving tablets (FDTs). The optimization process incorporates superdisintegrants like croscarmellose sodium, crospovidone, and sodium starch glycolate to facilitate rapid tablet disintegration and dissolution. Various excipients are assessed for mouthfeel, taste-masking, and tablet stability. The final formulation, prepared through direct compression, undergoes characterization for physical attributes, weight variation, hardness, friability, disintegration time, and drug content. In vitro dissolution studies reveal significantly improved drug release in Metoclopramide FDTs compared to conventional tablets, resulting in quicker absorption and onset of action. The optimized FDT formulation exhibits excellent performance in terms of physical characteristics, disintegration time, drug content, and dissolution rate. These findings indicate the potential of the formulated FDTs as a patient-friendly dosage form, offering enhanced therapeutic efficacy and faster relief from symptoms. Metoclopramide FDTs present a valuable alternative to conventional tablets, particularly beneficial for patients with swallowing difficulties or those requiring swift symptom relief. Subsequent investigations, including stability assessments and in vivo studies, are crucial for confirming the long-term stability, bioavailability, and therapeutic efficacy of the developed Metoclopramide fast-dissolving tablets.

Key words: Metoclopramide, fast-dissolving tablets, Formulation, Evaluation

Introduction

The formulation of drugs into a presentable form is a fundamental requirement in modern pharmaceuticals. Dosage forms serve as drug delivery systems for administering drugs to living organisms. Various types of dosage forms, such as tablets, syrups, suspensions, suppositories, injections, transdermal patches, employ different drug delivery mechanisms. While these classical and modern dosage forms have their advantages and disadvantages, creating an ideal drug delivery system remains a significant challenge for pharmacists. To achieve the desired therapeutic effect with minimal adverse effects, a thorough understanding of the physicochemical principles governing specific drug formulations is essential (Hannan et al., 2016).

Oral routes of drug administration are widely accepted, constituting approximately 50-60% of total dosage forms. Solid dosage forms, particularly tablets and capsules, are popular due to their ease of administration, accurate dosage, self-medication potential, and avoidance of pain. However, a common challenge arises for patients who find swallowing difficult. Water is typically required for swallowing oral dosage forms, and situations where water is not readily available, such as motion sickness, sudden coughing episodes, or allergic conditions, can pose challenges. Tablets designed to rapidly dissolve or disintegrate in the oral cavity have garnered considerable attention to address these issues (Bhowmik et al., 2009).

Swallowing difficulties are prevalent in certain populations, including geriatric patients with fears of choking, hand tremors, or dysphagia, as well as young individuals with underdeveloped muscular and nervous systems. Additionally, schizophrenic patients may experience poor compliance. Approximately one-third of the population, mainly pediatric and geriatric individuals, faces challenges in swallowing, leading to reduced compliance with oral tablet therapy and decreased overall treatment effectiveness.

Fast dissolving tablets (FDTs) have emerged as a solution to these challenges. The United States Food and Drug Administration (USFDA) defines FDTs as solid dosage forms containing a medicinal substance that disintegrates rapidly, typically within seconds when placed upon the tongue (Siddiqui et al., 2010).

Metoclopramide, a prescription medication, addresses various conditions of the stomach and intestines. Its uses include treating gastroparesis in people with diabetes, preventing nausea and vomiting induced by chemotherapy, and managing heartburn and esophageal reflux in individuals with gastroesophageal reflux disease (GERD). Metoclopramide functions by enhancing the muscle action in the upper digestive tract, aiding the quicker movement of food through the digestive system.

This project aims to formulate, develop, and evaluate Metoclopramide fast-dissolving tablets using polymers like HPMC, SSG, CP, CCS, and citric acid. Objectives include optimizing the formulation, assessing physicochemical and dissolution characteristics, determining drug release mechanisms, establishing in-vitro-in-vivo correlation, and evaluating the tablets.

Material and Methods

The preparation of fast-dissolving tablets of Metoclopramide (10mg) involved the direct compression method, incorporating various superdisintegrants to optimize the formulation. Croscarmellose sodium (Ac-Di-Sol) was included at concentrations of 10, 15, and 20 mg, and Crospovidone at concentrations of 10, 15, and 20 mg, aiming to determine the best formulation (Mohapatra et al., 2013). The following ingredients were accurately weighed, mixed geometrically in a dry mortar, and passed through a mesh 60.

The formulation included Magnesium stearate (6mg) as a lubricant, talc (5mg) as a glidant, and Microcrystalline cellulose as a bulking agent (109, 99, 89, 109, 99, and 89mg). This blend underwent analysis for pre-compression parameters, including Angle of repose, Bulk density, Tap density, Carr's index, and Hausner's ratio.

Subsequently, the blend was compressed using 8 mm (diameter) flat punches on a 'Rimek mini press 16 station rotary compression machine. Six formulations of Metoclopramide granules were prepared, each containing one of the three disintegrants at different concentrations. Tablets weighing 150 mg each were obtained, and the composition is detailed in Table no 1.

Table 1: Composition of Metoclopramide mouth dissolving tablets

Ingredients (mg)	Formulation code					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
Metoclopramide	10	10	10	10	10	10
Sodium Starch glycolate	10	15	20	-	-	-
Crospovidone	10	15	20	10	15	20
Croscarmellose sodium	-	-		10	15	20
Microcrystalline cellulose	109	99	89	109	99	89
Talc	5	5	5	5	5	5
Magnesium stearate	6	6	6	6	6	6
Total weight	150	150	150	150	150	150

Evaluation of Precompression Parameter

Angle of repose (θ): The angle of repose (θ) is a measure of the frictional forces within a loose powder or granules and represents the maximum angle between the surface of a pile of powder or granules and the horizontal plane (Carr et al., 1965). It is calculated using the formula:

$\theta = \tan^{-1}(hr)$ $\theta = \tan^{-1}(rh)$

Where θθ is the angle of repose, hh is the height, and rr is the radius. To measure the angle of repose, granules were allowed to flow through a funnel fixed to a stand at a defined height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

Loose bulk density (LBD) and tapped bulk density (TBD)

Loose bulk density (LBD) and tapped bulk density (TBD) were determined. A precisely weighed amount of granules was taken in a 50 ml capacity measuring cylinder and

tapped 100 times on a hard wooden surface. The LBD and TBD were calculated using the following formulas.

$$\text{LBD (Loose Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Volume of Packing}}$$

$$\text{TBD (Tapped Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Tapped Volume of Packing}}$$

Carr's Compressibility index: Percent compressibility of powder mix was determined by Carr's compressibility index (Ansel *et al.,* 1999), calculated by using following formula: -

$$\text{Carr's Index \%} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \times 100$$

Hausners ratio: It is determined by comparing tapped density to the bulk density by using following equation: -

Housner's ratio = Tapped bulk density/loose Bulk density

Hausner's ratio value <1.25 shows better flow properties

Evaluation of post compression Parameter

Shape and colour of tablets

Uncoated tablets were examined under a lens for the shape of the tablet and colour was observed by keeping the tablets in light.

Thickness test

Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and standard deviation was also calculated. The tablet thickness was measured using dial-caliper (Mitutoyo, Japan).

Weight variation test

Twenty tablets were selected randomly from each formulation and average weight was determined (USP, 2005). The tablets were weighed individually and compared with

average weight. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. The following percentage deviation in weight variation is allowed.

Hardness test

The hardness of tablet was measured by Pfizer hardness tester and results were expressed in Kg/cm^2.

Friability test

For this, 20 tablets were taken from each formulation and the friability was determined using Roche friabilator. The equipment was run for 4min at 25 revolutions per minute. The tablets were taken out, dedusted and reweighted and % friability was calculated. The friability was determined as the mass loss in percent according to Equation: -

$$\%\text{Friability} = (\text{Loss in weight}/\text{Initial weight}) \times 100$$

The test complies if tablets not loss more than 1% of their weight.

Uniformity of Drug Content: The uniformity of drug content test, essential for tablets with 10 mg or less weight of the active ingredient, was conducted as per Willard et al. (2007). Ten randomly selected tablets from each formulation (F1 to F6) were finely powdered, and drug equivalent to 10 mg was dissolved in 10 ml of phosphate buffer (pH 6.8). The solution was sonicated for 20 minutes, filtered through Whatman filter paper No. 41, and then 1 ml was diluted up to 100 ml with 0.1 N HCl. Drug content was determined spectrophotometrically at 274 nm.

Dissolution Rate Studies: In vitro drug release studies were carried out for the prepared tablets following the method outlined by Deepak et al. (2012). The dissolution studies were conducted using a USP XXII paddle-type Dissolution test apparatus. Tablets were evaluated in 900 ml dissolution medium stirred at 75 rpm and maintained at 37±0.2°C. The dissolution medium was sampled at different time intervals, and the volume withdrawn was compensated with an equal amount of fresh dissolution medium. The withdrawn samples were assayed spectrophotometrically at 274 nm using a UV-visible spectrophotometer.

Results and Discussion: The study aimed to develop and optimize Metoclopramide fast-dissolving tablets (10mg) using various superdisintegrants through the direct

compression method. The formulation sought to achieve optimal pre-compression and post-compression parameters, along with a quick disintegration time for improved patient compliance.

Pre-compression parameters, evaluating flow and compression characteristics, showed acceptable loose bulk density (0.345 to 0.382 gm/ml) and tapped bulk density (0.448 to 0.485 gm/ml). Carr's index indicated powder compressibility ranging from 18.55% to 25.36%, with Hausner's ratio values (1.228 to 1.340) confirming good flow properties.

Post-compression parameters demonstrated satisfactory tablet hardness (3.2 to 3.6 kg/cm^2) and low friability (0.658% to 0.778%). Weight variation test revealed minimal variation (148 to 153 mg), ensuring uniform tablet weight, and tablet thickness ranged from 1.25 to 1.33 mm, indicating consistent dimensions. Drug content analysis showed high percentages (97.56% to 99.45%), ensuring accurate dosing.

Disintegration time, a crucial parameter for rapid drug release, ranged from 68 to 95 seconds for all formulations. The formulation F3, containing 10 mg of croscarmellose sodium as the superdisintegrant, exhibited promising results with optimal pre-compression and post-compression parameters, making it a potential candidate for further development.

Table 2 : Results of pre-compression parameters of Metoclopramide

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
F1	0.345	0.448	22.99	1.299
F2	0.365	0.475	23.16	1.301
F3	0.358	0.463	22.68	1.293
F4	0.362	0.485	25.36	1.340
F5	0.382	0.469	18.55	1.228
F6	0.365	0.478	23.64	1.310

Table 3 : Results of post-compression parameters of all formulations

F. Code	Hardness test (kg/cm^2)	Friability (%)	Weight variation (%)	Thickness (mm)	Drug content (%)
F1	3.4±0.2	0.658±0.025	152±4	1.32±0.12	98.12±0.25
F2	3.5±0.1	0.778±0.023	148±3	1.31±0.14	97.65±0.15
F3	3.6±0.2	0.698±0.014	150±2	1.25±0.23	99.45±0.32
F4	3.4±0.2	0.715±0.025	153±4	1.29±0.14	98.65±0.17
F5	3.2±0.1	0.742±0.014	149±3	1.33±0.15	98.65±0.26
F6	3.2±0.4	0.745±0.012	153±2	1.25±0.23	97.56±0.32

Table 4: Results of disintegration time parameters of all formulations

Formulation code	Disintegration Time (Sec.) Mean ± SD
F1	95±3
F2	82±2
F3	68±4
F4	87±5
F5	80±3
F6	75±2

***Average of three determinations (n=3)**

Table 5 : *In-vitro* drug release data for optimized formulation F3

Time (min)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
1	1	0	42.36	1.627	57.64	1.761
5	2.24	0.698	63.32	1.802	36.68	1.564
10	3.16	1	82.25	1.915	17.75	1.249
15	3.87	1.176	98.74	1.994	1.26	0.100

Table 6 : Regression analysis data

Batch	Zero Order	First Order	Higuchi
	r^2		
F3	0.989	0.872	0.994

Conclusion

In summary, this study successfully developed and optimized fast-dissolving tablets of Metoclopramide using various superdisintegrants through the direct compression method. The assessment of pre-compression parameters, including loose bulk density, tapped bulk density, Carr's index, and Hausner's ratio, indicated favorable flow properties and compressibility of the powder blends.

Post-compression evaluation of the tablets yielded positive outcomes in terms of hardness, friability, weight variation, thickness, and drug content. The tablets exhibited commendable mechanical strength, low friability, uniform weight, accurate drug content, and consistent dimensions, affirming their quality and reliability.

The analysis of disintegration time showcased that all formulations possessed rapid disintegration properties, with short disintegration times ranging from 68 to 95 seconds. This attribute is pivotal for swift drug release and enhanced patient

compliance, particularly beneficial for individuals facing challenges in swallowing traditional tablets.

Among the formulations, F3, incorporating 10 mg of croscarmellose sodium as the superdisintegrant, emerged as the most promising. It displayed optimal pre-compression and post-compression parameters, coupled with rapid disintegration, positioning it as the preferred choice for fast-dissolving Metoclopramide tablets.

References

1. Hannan PA, Khan JA, Khan A, Safiullah S. Oral dispersible system: a new approach in drug delivery syste. Indian J Pharm Sci 2016;78:2-7.
2. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablet: an overview. J Chem Pharm Res 2009;1:163-77.
3. Siddiqui N, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization and evaluation: an overview. Int J Pharm Sci Rev Res 2010; 2:87-96.
4. Rajaram Mohapatra, Sibananda Senapati, Cinmaya Sahu, Sonali Mishra, Agnimitra Dinda, Alpha Mohapatra. Preparation and characterization of Irbesartan solid dispersion Tablet: Melt Dispersion Technique for dissolution enhancement. Der Pharmacia Lettre. 2013; 5(6):67-72.
5. Carr, R.L. *et al*., "Evaluating flow properties of solids". chem Engg. 1965; 72: 162-168.
6. Ansel HC., Allen LV., Popovich NG. Pharmaceutical dosage forms and drug delivery systems, Lippincott williams and wilkins, philadelphia. 1999, 60-63.
7. Hobart H. Willard, Lynne L. Merritt, John A. Dean, Frank A. settle. *et al.,* Instrumental methods of analysis. U Visible instrumentation.7th edition, Noida: India Binding House; 2007; 121-140.
8. G. Deepak, Raut Rahul, A. Senthil, M. Shanteshuday. Formulation and evaluation of irbesartan immediate release tablets. International research Journal of pharmacy. 2012, 3(4): 410-415.